

IN THE CLAIMS:

What we claim is:

1. (Currently Amended) A chemically synthesized double stranded short interfering ~~nucleic acid (siNA)~~ RNA (siRNA) molecule that directs cleavage of a huntingtin (HD) RNA comprising SEQ ID NO:3578 via RNA interference, wherein:
 - a. each strand of said siRNA molecule is about ~~19~~ 18 to about ~~23~~ 27 nucleotides in length;
 - b. one strand of said siRNA molecule comprises nucleotide sequence having sufficient complementarity to said HD RNA for the siRNA molecule to direct cleavage of the HD RNA via RNA interference; and
 - c. ~~at least one strand~~ one or more pyrimidine nucleotides present in one or both strands of said siRNA molecule ~~comprises one or more chemically modified nucleotides~~ is a 2'-deoxy-2'-fluoro pyrimidine nucleotide.
2. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 1, wherein said ~~siNA~~ siRNA molecule comprises no ribonucleotides.
3. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 1, wherein said ~~siNA~~ siRNA molecule comprises ribonucleotides.
4. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 1, wherein one of the strands of said double-stranded ~~siNA~~ siRNA molecule comprises a nucleotide sequence that is complementary to a nucleotide sequence of a said huntingtin (HD) gene or a portion thereof, and wherein the second strand of said double-stranded siRNA molecule comprises a nucleotide sequence substantially similar to the nucleotide sequence or a portion thereof of said huntingtin (HD) gene.
5. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 4, wherein each strand of the ~~siNA~~ siRNA molecule comprises about 19 to about 23 nucleotides, and wherein each strand comprises at least about 19 nucleotides that are complementary to the nucleotides of the other strand.

6. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 1, wherein said ~~siNA~~ siRNA molecule comprises an antisense region comprising a nucleotide sequence that is complementary to a nucleotide sequence of a said huntingtin (HD) gene or a portion thereof, and wherein said ~~siNA~~ siRNA further comprises a sense region, wherein said sense region comprises a nucleotide sequence substantially similar to the nucleotide sequence of said huntingtin (HD) gene or a portion thereof.
7. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 6, wherein said antisense region and said sense region each comprise about 19 to about 23 nucleotides, and wherein said antisense region comprises at least about 19 nucleotides that are complementary to nucleotides of the sense region.
8. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 1, wherein said ~~siNA~~ siRNA molecule comprises a sense region and an antisense region, and wherein said antisense region comprises a nucleotide sequence that is complementary to a nucleotide sequence of RNA encoded by a said huntingtin (HD) gene, or a portion thereof, and said sense region comprises a nucleotide sequence that is complementary to said antisense region.
9. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 6, wherein said ~~siNA~~ siRNA molecule is assembled from two separate oligonucleotide fragments wherein one fragment comprises the sense region and the second fragment comprises the antisense region of said ~~siNA~~ siRNA molecule.
10. (Currently Amended) The siRNA molecule of claim ~~claim~~ 6, wherein said sense region is connected to the antisense region via a linker molecule.
11. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 10, wherein said linker molecule is a polynucleotide linker.
12. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 10, wherein said linker molecule is a non-nucleotide linker.
13. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 6, wherein pyrimidine nucleotides in the sense region are 2'-O-methyl pyrimidine nucleotides.
14. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 6, wherein purine nucleotides in the sense region are 2'-deoxy purine nucleotides.

15. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 6, wherein the pyrimidine nucleotides present in the sense region are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
16. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 9, wherein the fragment comprising said sense region includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends of the fragment comprising said sense region.
17. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 16, wherein said terminal cap moiety is an inverted deoxy abasic moiety.
18. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 6, wherein the pyrimidine nucleotides of said antisense region are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
19. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 6, wherein the purine nucleotides of said antisense region are 2'-O-methyl purine nucleotides.
20. (Currently Amended) ~~20.~~—The ~~siNA~~ siRNA molecule of claim 6, wherein the purine nucleotides present in said antisense region comprise 2'-deoxy- purine nucleotides.
21. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 18, wherein said antisense region comprises a phosphorothioate internucleotide linkage at the 3' end of said antisense region.
22. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 6, wherein said antisense region comprises a glyceryl modification at the 3' end of said antisense region.
23. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 9, wherein each of the two fragments of said ~~siNA~~ siRNA molecule comprise 21 nucleotides.
24. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 23, wherein about 19 nucleotides of each fragment of the siRNA molecule are base-paired to the complementary nucleotides of the other fragment of the siRNA molecule and wherein at least two 3' terminal nucleotides of each fragment of the siRNA molecule are not base-paired to the nucleotides of the other fragment of the ~~siNA~~ siRNA molecule.
25. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 24, wherein each of the two 3' terminal nucleotides of each fragment of the ~~siNA~~ siRNA molecule are 2'-deoxy-pyrimidines.

26. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 25, wherein said 2'-deoxy-pyrimidine is 2'-deoxy-thymidine.
27. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 23, wherein all 21 nucleotides of each fragment of the ~~siNA~~ siRNA molecule are base-paired to the complementary nucleotides of the other fragment of the ~~siRNA~~ siRNA molecule.
28. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 23, wherein about 19 nucleotides of the antisense region are base-paired to the nucleotide sequence of the RNA encoded by a said huntingtin (HD) gene or a portion thereof.
29. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 23, wherein 21 nucleotides of the antisense region are base-paired to the nucleotide sequence of the RNA encoded by a said huntingtin (HD) gene or a portion thereof.
30. (Currently Amended) The ~~siNA~~ siRNA molecule of claim 9, wherein the 5'-end of the fragment comprising said antisense region optionally includes a phosphate group.
31. (Currently Amended) A pharmaceutical composition comprising the ~~siNA~~ siRNA molecule of claim 1 in an acceptable carrier or diluent.